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EXAMINER

NAFF, DAVID M

ART UNIT	PAPER NUMBER
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1651

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/03/24/1

Applicant(s)

Kragolin et al

Examiner

h. [signature]

Group Art Unit

1657

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

P r i d f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 10/1 + 10/10/02
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disp sition of Claims

- ☒ Claim(s) 1-4, 6-14, 18-53 + 89 is/are pending in the application.
- ☐ Of the above claim(s) _____ is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-4, 6-14, 18-53 + 89 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Applicati n Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____.
 - ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Other _____

Office Acti n Summary

The amendment of 10/1/02 has been entered. The amendment canceled claims 5, 17, 54-79 and 81-88, added claim 89, and amended claims 1, 2, 6, 7, 10, 12-14, 16, 18, 19, 23, 26, 27, 30-36, 38, 39, 44-47, 52 and 53.

Claims examined on the merits are 1-4, 6-16, 18-53 and 89 which are
5 all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being
10 indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Reciting "of the environment surrounding said crystal" makes the claim confusing since this is previously required in claim 1. A dependent claim should recite only how a previous claim is further
15 limited, and not be redundant by reciting a limitation already required in the previous claim. It is suggested that the above recitation be deleted.

Claim Rejections - 35 USC § 102

Claims 1-4, 6-16, 18-44, 46-53 and 89 are rejected under 35
20 U.S.C. 102(a) as anticipated by Navia et al (5,618,710) for the type of reasons set forth in the previous office action of 4/1/02, and reiterated below.

The claims are drawn to multifunctional agent crosslinked protein crystals that are capable of controlled dissolution from insoluble form
25 to soluble active form upon a change in environment surrounding the

crystals selected from the group consisting of change in temperature, change in pH, change in chemical composition, change from concentrate to dilute form, and combinations thereof.

Navia et al disclose multifunctional agent crosslinked protein
5 crystals that are inherently capable of being changed to soluble form as claimed by one or more of the claimed environmental changes since crosslinked protein crystals of Navia et al can be prepared using crosslinking conditions that will result in essentially the same or less crosslinking than obtained when using crosslinking conditions disclosed
10 in the present specification. For example, in Navia et al in example 2 (col 37, lines 32-35), 12.5% glutaraldehyde is used for 3 hours, in example 4 (col 43, lines 48-52), 5.77% glutaraldehyde is used for one hour, in example 5 (col 44, lines 56-61) and 6 (col 45, lines 64-67), 12.5% glutaraldehyde is used for one hour, in example 7 (col 46, lines
15 50-55), 24% glutaraldehyde is used for 20 minutes, in example 9 (col 48, line 40), 2% glutaraldehyde is used, and in example 10 (col 51, lines 15-18), 7.5% glutaraldehyde is used for 30 minutes. In the present specification, in example 18, the final glutaraldehyde concentration is 4% and crosslinking is for 24 hours. These conditions appear to also be
20 used in examples 19 and 20. In example 22, 6.5% glutaraldehyde is used for one hour and in example 23, 6.0% glutaraldehyde is used for one hour. Thus, it is apparent that the crosslinking conditions used by Navia et al are essentially equivalent to those disclosed by the present specification and would not have resulted in a substantially greater
25 amount of crosslinking. While Navia et al may use a higher amount of

crosslinking agent in certain instances, the time for crosslinking is less than disclosed in the present specification when using a lower amount of crosslinking agent. Using 7.5% glutaraldehyde for 30 minutes or 5.77% glutaraldehyde for one hour as in Navia et al is not going to result in more crosslinking than when using 6.5% or 6.0% glutaraldehyde for one hour or using 4% glutaraldehyde for 24 hours as in the present specification. Similarly, using 24% glutaraldehyde for 20 minutes or 12.5% glutaraldehyde for one hour will not result in substantially more crosslinking than using 4% glutaraldehyde for 24 hours.

Response to Arguments

Applicant's arguments filed 10/1/02 have been fully considered but they are not persuasive.

Applicants have presented a Declaration by Bhami C. Shenoy (filed 10/10/02), and urge that the declaration shows that the crosslinked protein crystals of Navia et al are not inherently capable of changing from insoluble to soluble form when subjected to the same change in environment that causes dissolution of the crosslinked protein crystals according to the present application.

However, the declaration is unpersuasive since dissolution results show substantial inconsistency when using the same or essentially the same crosslinking conditions of examples in the application. For example, Examples 18-20 shown by Table 2 appear to use the same crosslinking conditions to produce crosslinked lipase crystals, yet the amount of crosslinked lipase crystals dissolving ranges from 60% to 42% at 3 hr and from 100% to 49% at 24 hr. In Table 3, the crosslinked

lipase crystals of Examples 22 and 23 are prepared under essentially the same conditions while dissolution ranges from 63% to 17% at 3 hr and from 100% to 69% at 24 hr. These results indicate there is wide deviation in dissolution when using the same or essentially the same crosslinking
5 conditions. When carrying out dissolution tests with crosslinked enzyme crystals prepared according to examples of Navia et al, multiple crosslinked enzyme crystals prepared under the same conditions according to each example have not been tested for dissolution to determined the amount of deviation when using the same crosslinking conditions. The
10 deviation could be the same as when carrying out the examples of the present application, and therefore on repeated tests the dissolution may not have been 0%, or .12% to .25% as shown by the declaration.

It is noted that in Example 9 of Navia et al when using 2% crosslinker, the time of crosslinking is not disclosed, and the
15 declaration does not disclose a crosslinking time when repeating this example. The crosslinking time used in the test of the declaration should have been specified.

In Table 3 of the declaration, Examples 22 and 23 use 6.5% and 6.0% crosslinker for 1 hr to obtain 17% to 100% dissolution, yet show 0%
20 dissolution when using 7.5% crosslinker for 30 minutes as in Example 10 of Navia et al. Using 1% and 1.5% greater crosslinker for a shorter time of 30 minutes as in Navia et al would not appear to result in the difference in dissolution shown by the declaration.

It is further pointed out that PeptiCLECTM-TR in Table 2 of the
25 declaration results in .21% dissolution at 3 hr and .25% dissolution at

24 hr. While this amount of dissolution is small, the claims do not require a greater amount of dissolution. Additionally, the amount of dissolution for PeptiCLEC™-TR increased from 3 hr to 24 hr, and longer times would have appeared to result in a greater amount of dissolution and even complete dissolution if the time had been long enough. The claims do not limit the amount of time in which dissolution can occur.

Claim Rejections - 35 USC § 103

Claim 45 is rejected under 35 U.S.C. 103(a) as being unpatentable over Navia et al.

10 The claim requires a detergent formulation containing the crosslinked protein crystal.

It would have been obvious to use a crosslinked enzyme crystal such as a protease produced as disclosed by Navia et al in a detergent formulation since it is conventional to use enzymes such as proteases in detergent formulations and Navia et al disclose using crosslinked enzyme crystals for uses where enzymes are conventionally used.

Response to Arguments

Applicants rely on the Shenoy Declaration to traverse this rejection, and the declaration is unpersuasive for reasons set forth above.

Claim Rejections - 35 USC § 103

Claims 1-4, 6-16, 18-53 and 89 are rejected under 35 U.S.C. 103(a) as being unpatentable over Navia et al in view of Neville et al (5,066,490) and Kausch et al (5,508,164).

Neville et al disclose using reversible crosslinking agents for linking an amino group containing substance to a group on a second compound so the crosslinking agent can be cleaved to release the substance.

5 Kausch et al disclose using disulfide crosslinking agents for reversible immobilization (col 6, lines 52-68).

It would have been obvious to use a reversible crosslinking agent such as a disulfide crosslinking agent as the crosslinking agent of Navia et al to obtain reversible immobilization as suggested by Neville et al
10 and Kausch et al. When using a reversible crosslinker, it would have been obvious that the crosslinked crystals can be dissolved by cleaving the crosslinker, and it would have been obvious to release the crosslinked protein of Navia et al in soluble form for the same type of reasons that Neville et al and Kausch et al desire to release a substance
15 crosslinked to another substance.

Response to Arguments

The Shenoy Declaration does not obviate this rejection since the rejection is not based on the crosslinked crystals of Navia et al being inherently capable of change from insoluble to soluble form. The
20 rejection is instead based on it being obvious to obtain this change in solubility by using a reversible crosslinker as suggested by the secondary references.

Double Patenting

Claims 1-4, 6-16, 18-53 and 89 are rejected under the judicially
25 created doctrine of obviousness-type double patenting as being

unpatentable over claims 1-19 of U.S. Patent No. 6,140,475. Although the conflicting claims are not identical, they are not patentably distinct from each other because crosslinked protein crystals that dissolve as presently claimed would have been obvious from the method of the claims
5 of the patent that produces crosslinked crystals that dissolve as a result of a change in environment that can be the same as required by the present claims.

Applicants indicate they stand ready to file a Terminal Disclaimer, if appropriate, upon an indication of allowable subject matter.

10 **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of
15 this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the
20 statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is (703) 308-0520. The examiner can normally be reached on

Monday-Thursday and every other Friday from about 8:30 AM to about 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, a message can be left on voice mail.


5 If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn, can be reached at telephone number (703) 308-4743.

The fax phone number is (703) 872-9306 before final rejection or (703) 872-9307 after final rejection.

10 Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

15

DMN
12/12/02


DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 12857